

What is claimed is:

1. A method of preparing (S)-chiral alcohol comprising:

(a) reacting in organic solvent a compound of the following chemical formula 1 as a starting material,

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a racemization metal catalyst,

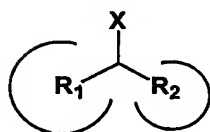
an acyl donor being capable of acylating an alcohol compound, and

a protein hydrolysis enzyme being capable of stimulating the enantioselective acylation of a racemic compound to obtain a chiral ester compound of chemical formula 3; and

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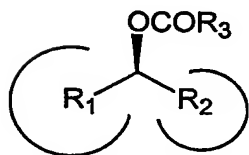
(b) hydrolyzing the chiral ester compound of chemical formula 3 to obtain (S)-chiral alcohol;

[chemical formula 1]



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[chemical formula 3]



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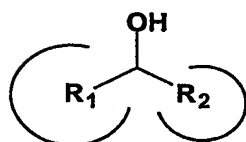
wherein X is -OH or =O, R₁, R₂ and R₃ are independently substituted or unsubstituted C₁-C₁₅ alkyl, substituted or unsubstituted C₂-C₁₅ alkenyl, substituted or unsubstituted C₂-C₁₅ alkynyl, substituted or unsubstituted C₅-C₁₈ aryl, substituted or unsubstituted C₆-C₁₈ arylalkyl, substituted or unsubstituted C₂-C₂₀ heterocycle, substituted or unsubstituted C₃-C₂₀ heteroarylalkyl, substituted or unsubstituted C₃-C₁₅ cycloalkyl, substituted or unsubstituted C₃-C₁₅ cycloalkenyl, substituted or unsubstituted C₆-C₁₅ cycloalkynyl, or substituted or unsubstituted C₃-C₂₀ heterocycloalkyl, wherein the R₁ group and the R₂ group can be linked together, and wherein a size of a circular arc indicates that the R₁ group is larger than the R₂ group.

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2. The method of preparing (S)-chiral alcohol according to claim 1, further comprising adding a hydrogen donor in the (a) step when the starting material of chemical formula 1 comprises ketone such that X is =O.

3. The method of preparing (S)-chiral alcohol according to claim 1: wherein the starting material of chemical formula 1 is the compound of the following chemical formula 1a;

[chemical formula 1a]



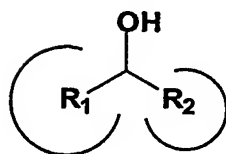
wherein R₁ and R₂ are independently substituted or unsubstituted C₁-C₁₅ alkyl, substituted or unsubstituted C₂-C₁₅ alkenyl, substituted or unsubstituted C₂-C₁₅ alkynyl, substituted or unsubstituted C₅-C₁₈ aryl, substituted or unsubstituted C₆-C₁₈ arylalkyl, substituted or unsubstituted C₂-C₂₀ heterocycle, substituted or unsubstituted C₃-C₂₀ heteroarylalkyl, substituted or unsubstituted C₃-C₁₅ cycloalkyl, substituted or unsubstituted C₃-C₁₅ cycloalkenyl, substituted or unsubstituted C₆-C₁₅ cycloalkynyl, or substituted or unsubstituted C₃-C₂₀ heterocycloalkyl; and

wherein R₁ and R₂ can be linked together.

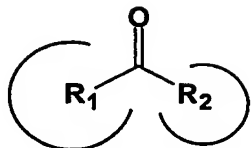
4. The method of preparing (S)-chiral alcohol according to claim 3, further comprising:

obtaining an alcohol compound of chemical formula 1a by adding hydrogen donor to ketone compound of the following chemical formula 1b to reduce it;

[chemical formula 1a]



[chemical formula 1b]



wherein R_1 and R_2 are independently substituted or unsubstituted C_1 - C_{15} alkyl, substituted or unsubstituted C_2 - C_{15} alkenyl, substituted or unsubstituted C_2 - C_{15} alkynyl, substituted or unsubstituted C_5 - C_{18} aryl, substituted or unsubstituted C_6 - C_{18} arylalkyl, substituted or unsubstituted C_2 - C_{20} heterocycle, substituted or unsubstituted C_3 - C_{20} heteroarylalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkenyl, substituted or unsubstituted C_6 - C_{15} cycloalkynyl, or substituted or unsubstituted C_3 - C_{20} heterocycloalkyl; and

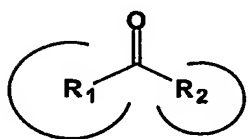
wherein R_1 and R_2 can be linked together.

5. The method of preparing (S)-chiral alcohol according to claim 1, further comprising:

adding hydrogen donor to reduce a ketone group in (a) step;

wherein the compound of chemical formula 1 comprises chemical formula 1b;

[chemical formula 1b]



wherein R_1 and R_2 are independently substituted or unsubstituted C_1 - C_{15} alkyl, substituted or unsubstituted C_2 - C_{15} alkenyl, substituted or unsubstituted C_2 - C_{15} alkynyl, substituted or unsubstituted C_5 - C_{18} aryl, substituted or unsubstituted C_6 - C_{18} arylalkyl, substituted or unsubstituted C_2 - C_{20} heterocycle, substituted or unsubstituted C_3 - C_{20} heteroarylalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkenyl, substituted or unsubstituted C_6 - C_{15} cycloalkynyl, or substituted or unsubstituted C_3 - C_{20} heterocycloalkyl; and

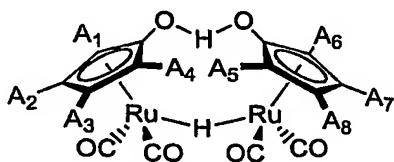
wherein R_1 and R_2 can be linked together.

6. The method of preparing (S)-chiral alcohol according to claim 1, wherein the (a) step reaction comprises a one-pot reaction and wherein the reaction is performed in one vessel.

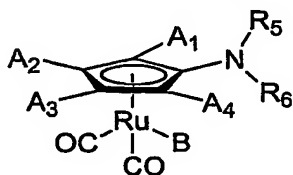
7. The method of preparing (S)-chiral alcohol according to claim 1, wherein the metal catalyst comprises a ruthenium complex compound.

8. The method of preparing (S)-chiral alcohol according to claim 1, wherein the metal catalyst is selected from the group consisting of ruthenium complex compounds represented by the following chemical formulas 4 to 8:

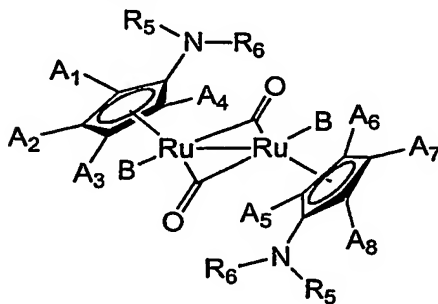
[chemical formula 4]



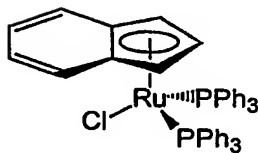
[chemical formula 5]



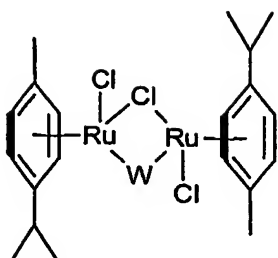
[chemical formula 6]



[chemical formula 7]



[chemical formula 8]



wherein A_1 , A_2 , A_3 , A_4 , A_5 , A_6 , A_7 and A_8 are independently hydrogen, substituted or unsubstituted C_1 - C_{10} alkyl, substituted or unsubstituted C_5 - C_{18} aryl, or substituted or unsubstituted C_2 - C_{20} heterocycle;

5 wherein R_5 and R_6 are independently hydrogen, substituted or unsubstituted C_1 - C_{15} alkyl, substituted or unsubstituted C_2 - C_{15} alkenyl, substituted or unsubstituted C_2 - C_{15} alkynyl, substituted or unsubstituted C_5 - C_{18} aryl, substituted or unsubstituted C_6 - C_{18} arylalkyl, substituted or unsubstituted C_2 - C_{20} heterocycle, substituted or unsubstituted C_3 - C_{20} heteroarylalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkenyl, substituted or unsubstituted C_6 - C_{15} cycloalkynyl, or substituted or unsubstituted C_3 - C_{20} heterocycloalkyl;

wherein B comprises a substituent selected from the group consisting of hydrogen, carbonyl, halogen and trifluoromethanesulfonate or there is no substituent in B site; and

15 wherein W is hydrogen or a halogen.

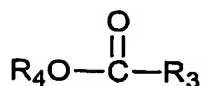
9. The method of preparing (S)-chiral alcohol according to claim 2, wherein the acyl donor comprises 2,4-dimethyl-3-pentanol, 2,6-dimethyl-4-heptanol, formic acid, or hydrogen.

10. The method of preparing (S)-chiral alcohol according to claim 1, wherein the acyl donor is linked to the R_1 group or the R_2 group of the chemical formula 1.

11. The method of preparing (S)-chiral alcohol according to claim 10, wherein the acyl donor is a substituent including $-OCO-R_3$ terminal group linked to the R_1 or R_2 of the chemical formula 1.

12. The method of preparing (S)-chiral alcohol according to claim 1, wherein the acyl donor is the compound of the chemical formula 2; and

[chemical formula 2]



wherein R₃ and R₄ are independently substituted or unsubstituted C₁-C₁₅ alkyl, substituted or unsubstituted C₂-C₁₅ alkenyl, substituted or unsubstituted C₂-C₁₅ alkynyl, substituted or unsubstituted C₅-C₁₈ aryl, substituted or unsubstituted C₆-C₁₈ arylalkyl, substituted or unsubstituted C₂-C₂₀ heterocycle, substituted or unsubstituted C₃-C₂₀ heteroarylalkyl, substituted or unsubstituted C₃-C₁₅ cycloalkyl, substituted or unsubstituted C₃-C₁₅ cycloalkenyl, substituted or unsubstituted C₆-C₁₅ cycloalkynyl, or substituted or unsubstituted C₃-C₂₀ heterocycloalkyl.

13. The method of preparing (S)-chiral alcohol according to claim 1, wherein the protein hydrolysis enzyme is selected from the group consisting of stabilized or fixed subtilisin, chymotrypsin, papain, protease from *Aspergillus oryzae*, protease from *Aspergillus melleus*, protease from *Streptomyces griseus*, and protease from *Bacillus stearothermophilus*.

14. The method of preparing (S)-chiral alcohol according to claim 1, wherein the protein hydrolysis enzyme is subtilisin.

15. The method of preparing (S)-chiral alcohol according to claim 1, wherein the organic solvent is benzene, toluene, C₅-C₁₀ alkane, C₅-C₁₀ cycloalkane, tetrahydrofuran, dioxane, C₂-C₁₀ dialkylether, C₃-C₁₀ alkylate, C₂-C₁₀ cyanoalkane, C₃-C₁₀ dialkyl ketone, dichloromethane, chloroform, carbon tetrachloride, C₄-C₁₀ tertiary alcohol, or a room temperature ionic liquid.

16. The method of preparing (S)-chiral alcohol according to claim 1, wherein the reaction temperature in (a) step is room temperature to 80°C.

17. A (S)-chiral alcohol prepared according to claim 1.

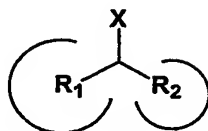
18. A method of preparing (S)-chiral ester comprising:
25 reacting in organic solvent the compound of the following chemical formula 1 as a starting material,

a racemization metal catalyst,

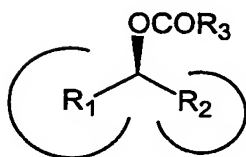
an acyl donor being capable of acylating an alcohol compound, and

a protein hydrolysis enzyme being capable of stimulating the
30 enantioselective acylation of a racemic compound to obtain a chiral ester compound of chemical formula 3.

[chemical formula 1]



[chemical formula 3]



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wherein R_1 and R_2 are independently substituted or unsubstituted C_1 - C_{15} alkyl, substituted or unsubstituted C_2 - C_{15} alkenyl, substituted or unsubstituted C_2 - C_{15} alkynyl, substituted or unsubstituted C_5 - C_{18} aryl, substituted or unsubstituted C_6 - C_{18} arylalkyl, substituted or unsubstituted C_2 - C_{20} heterocycle, substituted or unsubstituted C_3 - C_{20} heteroarylalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkenyl, substituted or unsubstituted C_6 - C_{15} cycloalkynyl, or substituted or unsubstituted C_3 - C_{20} heterocycloalkyl, and R_1 and R_2 can be linked together; and

wherein a size of a circular arc indicates that the R_1 group is larger than the R_2 group.

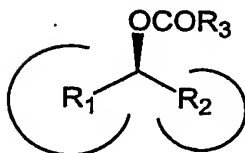
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19. The method of preparing (S)-chiral ester according to claim 18, further comprising adding a hydrogen donor in the (a) step and when the starting material comprises ketone where $X = O$.

20. A (S)-chiral ester of the following chemical formula 3 prepared according to claim 18;

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[chemical formula 3]



wherein R_1 , R_2 and R_3 are independently substituted or unsubstituted C_1 - C_{15} alkyl, substituted or unsubstituted C_2 - C_{15} alkenyl, substituted or unsubstituted C_2 - C_{15} alkynyl, substituted or unsubstituted C_5 - C_{18} aryl, substituted or unsubstituted C_6 - C_{18} arylalkyl, substituted or unsubstituted C_2 - C_{20} heterocycle, substituted or unsubstituted C_3 - C_{20} heteroarylalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkyl, substituted or unsubstituted C_3 - C_{15} cycloalkenyl, substituted or unsubstituted C_6 - C_{15} cycloalkynyl, or substituted or unsubstituted C_3 - C_{20} heterocycloalkyl;

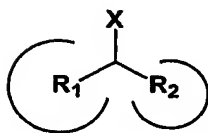
wherein the R_1 group and the R_2 group can be linked together; and

wherein a size of a circular arc indicates that the R_1 group is larger than the R_2 group.

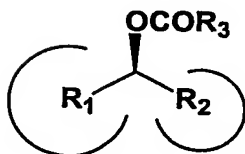
21. A method of preparing (S)-chiral alcohol of the following chemical formula 1 comprising:

hydrolyzing the chiral ester of the chemical formula 3 prepared according to claim 18.

[chemical formula 1]



[chemical formula 3]



wherein X -OH or =O,

wherein R_1 , R_2 and R_3 are independently substituted or unsubstituted C_1 - C_{15} alkyl, substituted or unsubstituted C_2 - C_{15} alkenyl, substituted or unsubstituted C_2 - C_{15} alkynyl, substituted or unsubstituted C_5 - C_{18} aryl, substituted or unsubstituted C_6 - C_{18} arylalkyl, substituted or unsubstituted C_2 - C_{20} heterocycle, substituted or

unsubstituted C₃-C₂₀ heteroarylalkyl, substituted or unsubstituted C₃-C₁₅ cycloalkyl, substituted or unsubstituted C₃-C₁₅ cycloalkenyl, substituted or unsubstituted C₆-C₁₅ cycloalkynyl, or substituted or unsubstituted C₃-C₂₀ heterocycloalkyl;

wherein R₁ and R₂ can be linked together; and

5 wherein a size of a circular arc indicates that the R₁ group is larger than the R₂ group.